

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

553, 118

PCT/JP2004/004612



Applicant's or agent's file reference 09624	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2004/004612	International filing date (day/month/year) 31 March 2004 (31.03.2004)	Priority date (day/month/year) 15 April 2003 (15.04.2003)
International Patent Classification (IPC) or national classification and IPC C12N 5/06, 5/10, 15/09, A61K 48/00, A01K 67/027		
Applicant KYOTO UNIVERSITY		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

a. ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:

☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒ Box No. I Basis of the report

☐ Box No. II Priority

☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

☐ Box No. IV Lack of unity of invention

☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

☐ Box No. VI Certain documents cited

☐ Box No. VII Certain defects in the international application

☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 08 November 2004 (08.11.2004)	Date of completion of this report 16 June 2005 (16.06.2005)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/004612

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claim No. 18

because:

☒ the said international application, or the said claim No. 18
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim No. 18

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the
Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with
the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/004612

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-11, 14-16, 19-27	YES
	Claims	12, 13, 17	NO
Inventive step (IS)	Claims	1-11, 14-16, 19-27	YES
	Claims	12, 13, 17	NO
Industrial applicability (IA)	Claims	1-17, 19-27	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Life Science Fukko Zaidan Nenpo, 2002 Edition (March 1, 2003), pp. 17-19
 Document 2: Cell Mol Life Sci, Vol. 58, no. 8, pp.1061-1066 (2001)
 Document 3: Science, Vol. 287, No. 5457, pp. 1489-1493 (2000)
 Document 4: Gendai Kagaku Zokan 41, Saisei Igaku/Saisei Iryo (July 1, 2002), pp. 24-28
 Document 5: Proc Natl Acad Sci USA, Vol. 98, No. 23, pp. 13090-13095 (2001)
 Document 6: FEBS Lett, Vol. 475, No. 1, pp. 7-10 (2000)

Claims 1-11, 14-16 and 19-27

The inventions of Claims 1-11, 14-16 and 19-27 appear to possess novelty and involve an inventive step based on the documents cited in the ISR.

Document 1 describes that in culturing and maintaining ES cells, maintaining cells in an undifferentiated state while maintaining differentiation pluripotential is complicated even if LIF, a cell differentiation inhibitory factor, is used; it also states that an investigation was conducted using a seminiferous tubule *in vitro* transplant means, of whether spermatogonia sustained and grown with the addition of GDNF (glial cell line-derived neurotrophic factor) have the functions of stem cells.

Document 2 describes that stem cell differentiation in spermatogenesis is controlled by GDNF and IL-6 family LIF.

Document 3 describes that GDNF controls auto-proliferation and differentiation of undifferentiated spermatogonia including sperm stem cells.

Documents 5 and 6 describe a means for producing a transgenic mouse by introducing an exogenous gene in a sperm stem cell using a retrovirus.

However, none of the documents describes growing *in vitro*, in a culture medium containing GDNF or LIF, of cells judged to be "sperm stem cells" based on measurement of the stem cell functions such as colony formation by seminiferous tubule transplant; further, as it was common general technical knowledge at the time of this application that growth of sperm stem cells could not be induced using GDNF or LIF, as is described in the referenced document presented by the applicant, (Biology of Reproduction, Vol. 68, pp. 2207-2214 (2003)), growth of "sperm stem cells" *in vitro* with in a culture medium containing GDNF or LIF could not easily be conceived by a person skilled in the art.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Box V:

Claims 12, 13 and 17

The inventions of Claims 12, 13 and 17 do not appear to possess novelty based on document 4 cited in the ISR.

Document 4 describes that the spermatogenesis function was obtained by transplanting sperm stem cells to a testicle.

(In the written reply dated February 14, 2005, it is asserted that the "sperm stem cell in Claims 12, 13 and 17 are grown by culturing using a culture medium that contains GDNF or its equivalent substance and LIF," but because it must be interpreted that sperm stem cells obtained by any means, not just the culturing means of the invention of this application, must be interpreted to be included in the scope of the claims, the subject matter cannot be considered novel unless a clear distinction is made in comparison with the "sperm stem cells" described in Document 4 by, for example, specific cell surface markers and such.)